

**A Selected History of Behavioral Clinical
Trials:
What Have We Learned?**

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“The wrong view of science betrays
itself in the craving to be right.”

Karl Popper,
The Logic of Scientific Discovery, 1934

HYPOTHESES


- **Medicine / Epidemiology:**

The policy of offering the intervention results in improvement in the clinical endpoint.

- **Behavioral Sciences:**

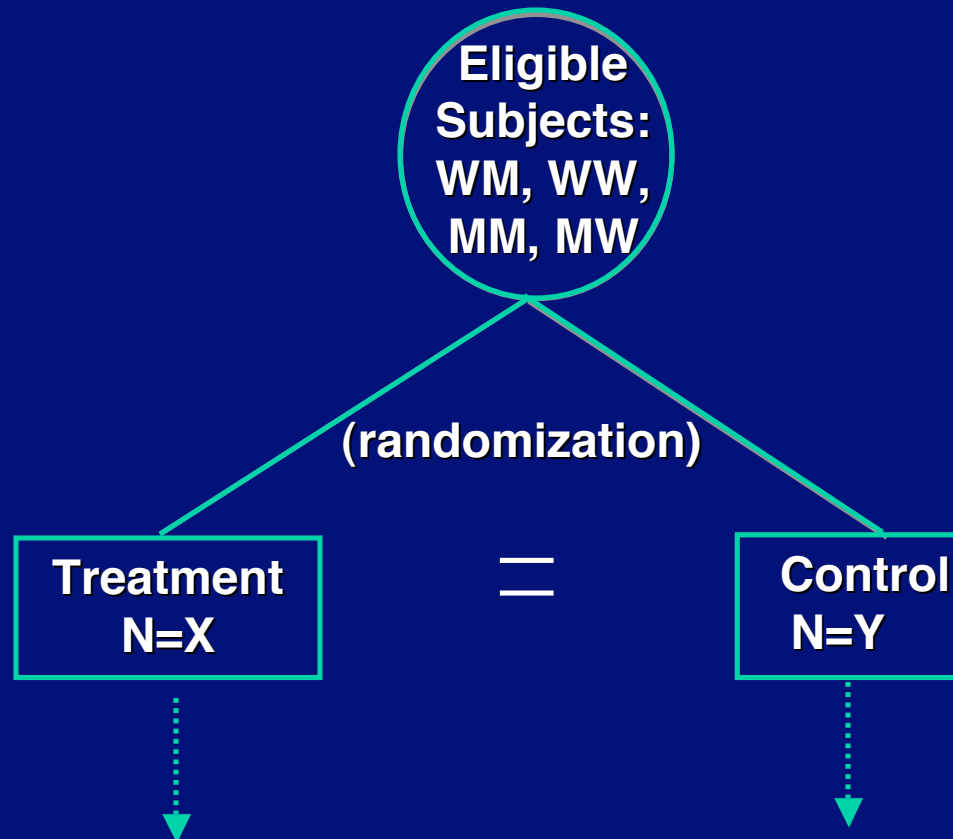
Improvement in the behavioral risk factor results in improvement in the clinical endpoint.

Clinical Trial Design

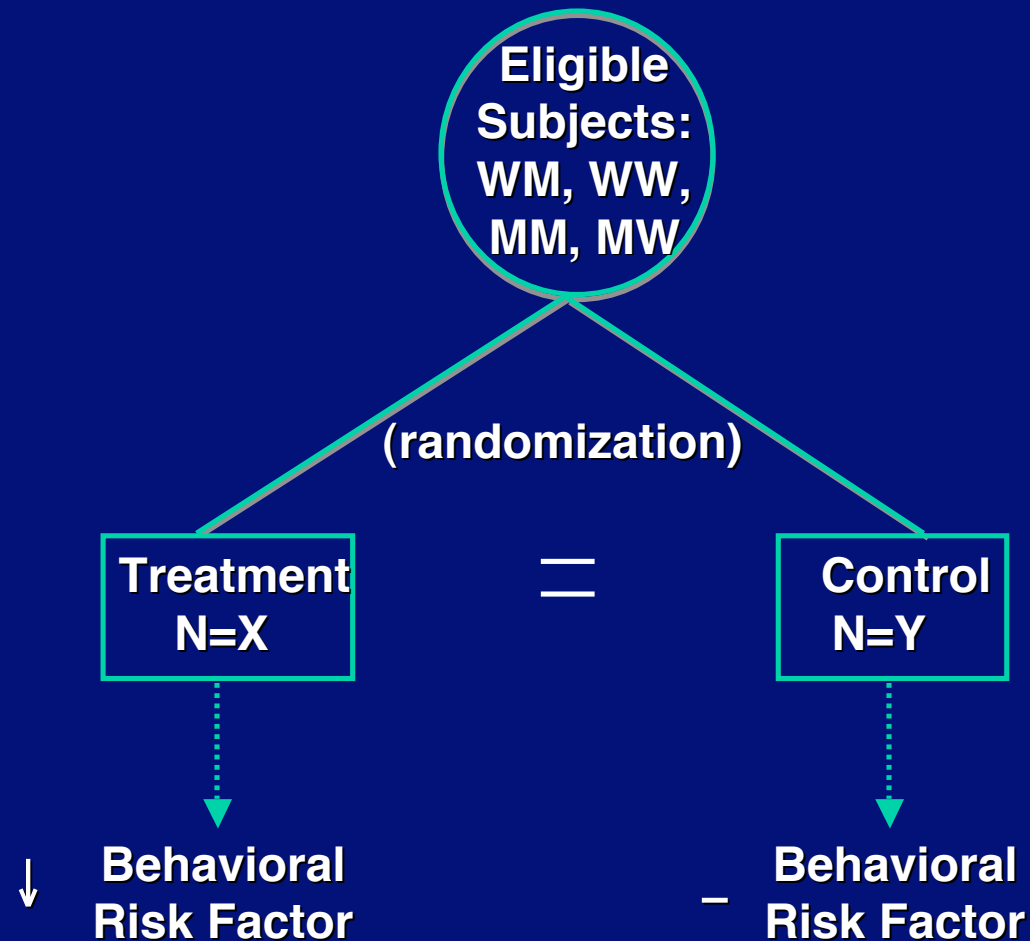


**Eligible
Subjects:
WM, WW,
MM, MW**

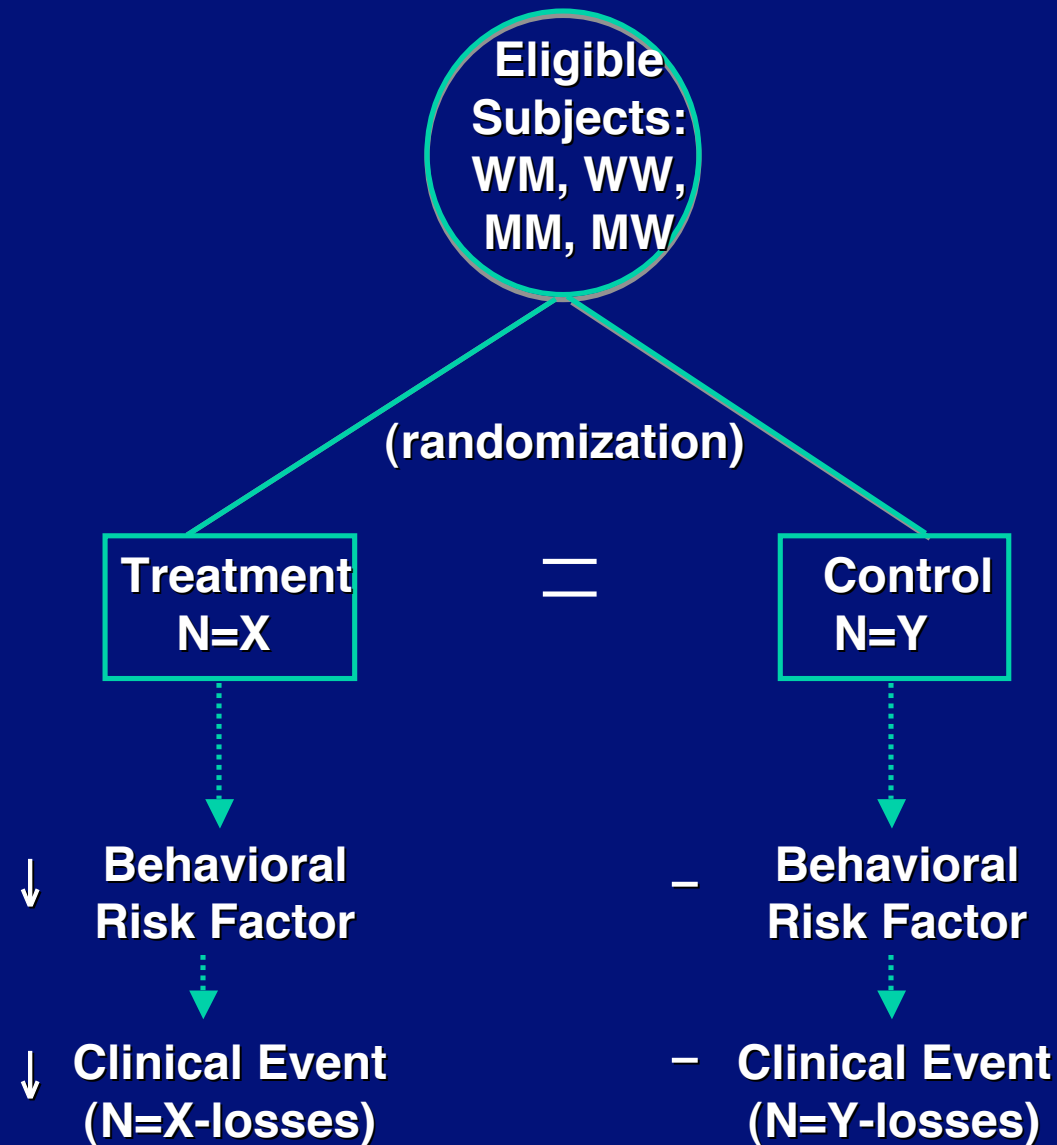
Clinical Trial Design



Clinical Trial Design



Clinical Trial Design



The Recurrent Coronary Prevention Project 1977-1985

Principal Investigator: Meyer Friedman, MD

HYPOTHESIS: Type A behavior can be reduced and this reduction will result in reduced cardiac deaths or nonfatal MI.



"If you can't relax, pretend to relax."

I. 1. Walk more slowly than wife/friend

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2. Speak more slowly

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3. Eat more slowly

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4. Discontinue fist clenching/knee jiggling

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5. Leave watch off 2 of 5 working days

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6. Seek longest line in bank/shop

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7. Linger at table

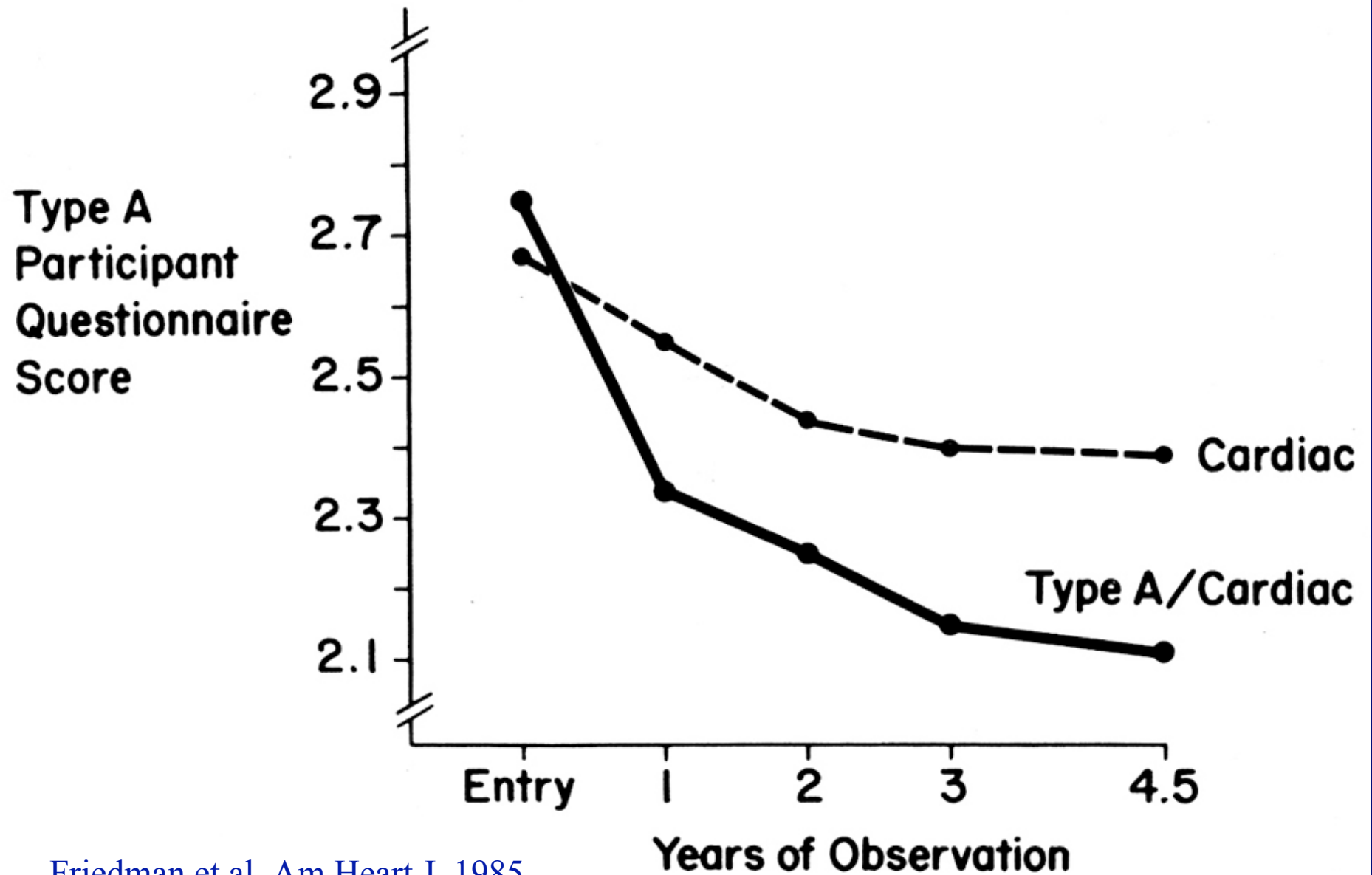
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help



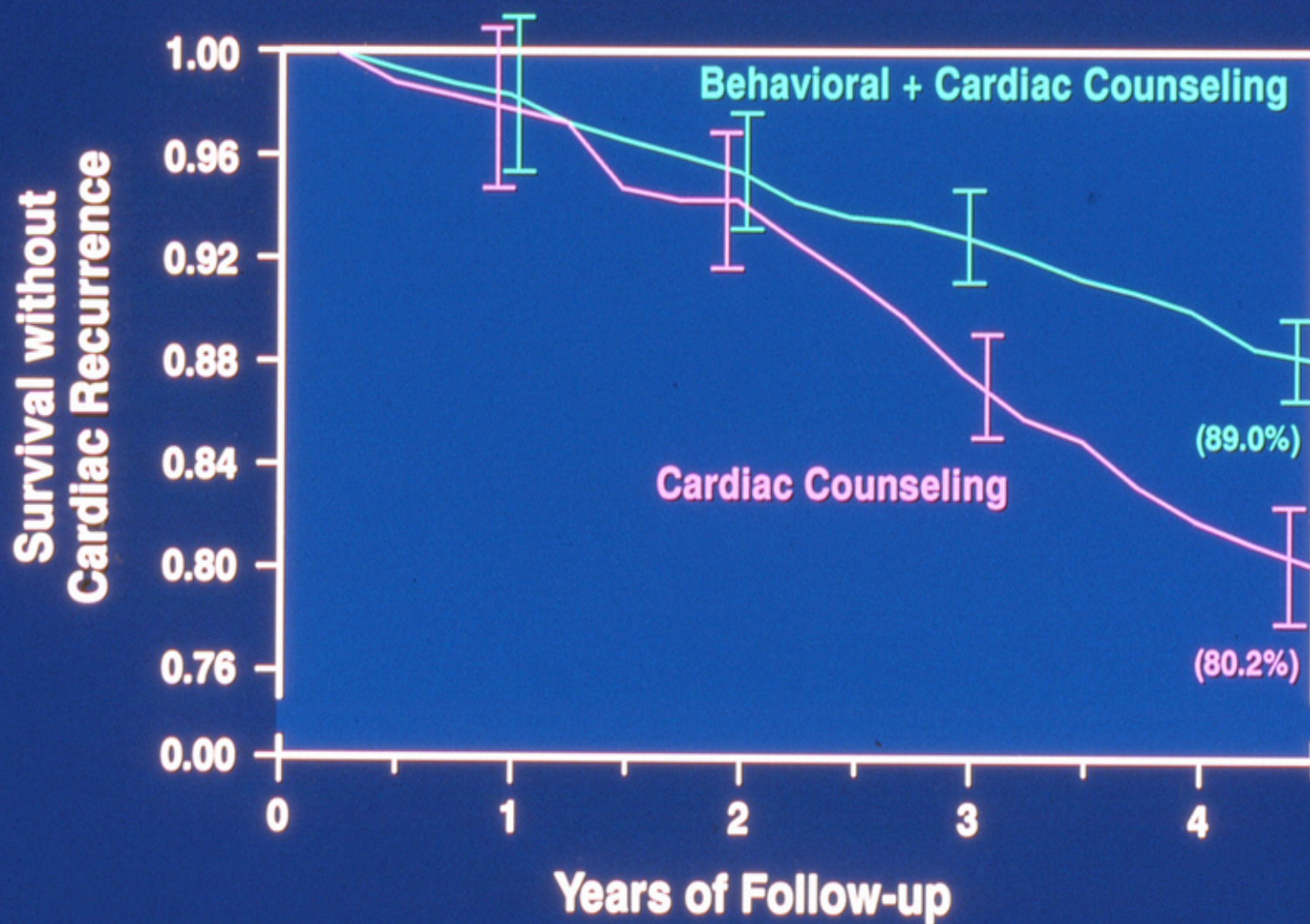
OFF HAND,
I'D SAY
YOU'RE
HOOKED!



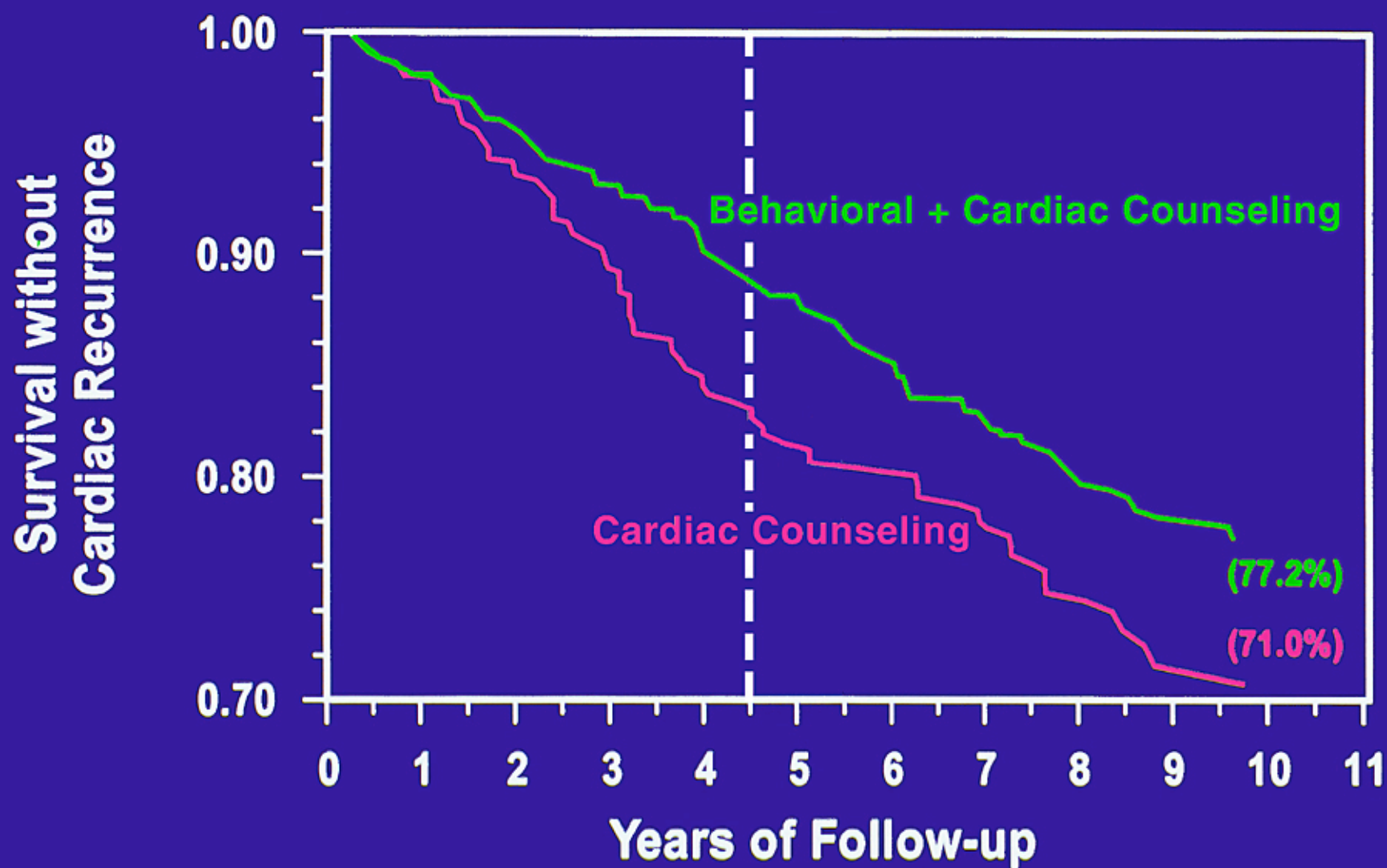


Friedman et al, Am Heart J, 1985

Cardiac Recurrence at 4.5 Years



Cardiac Recurrence at 8.5 Years



Impact of RCPP Intervention on Psychosocial Risk Factors

	Improved at End of Treatment	Improvement Predicted Subsequent CHD Events
Type A Behavior	***	ns
Hostility	***	ns
Anger	***	ns
Impatience	***	ns
Life Satisfaction	***	ns
Self-Efficacy at Managing Stress	***	*
Social Support	***	ns
Depression	***	**

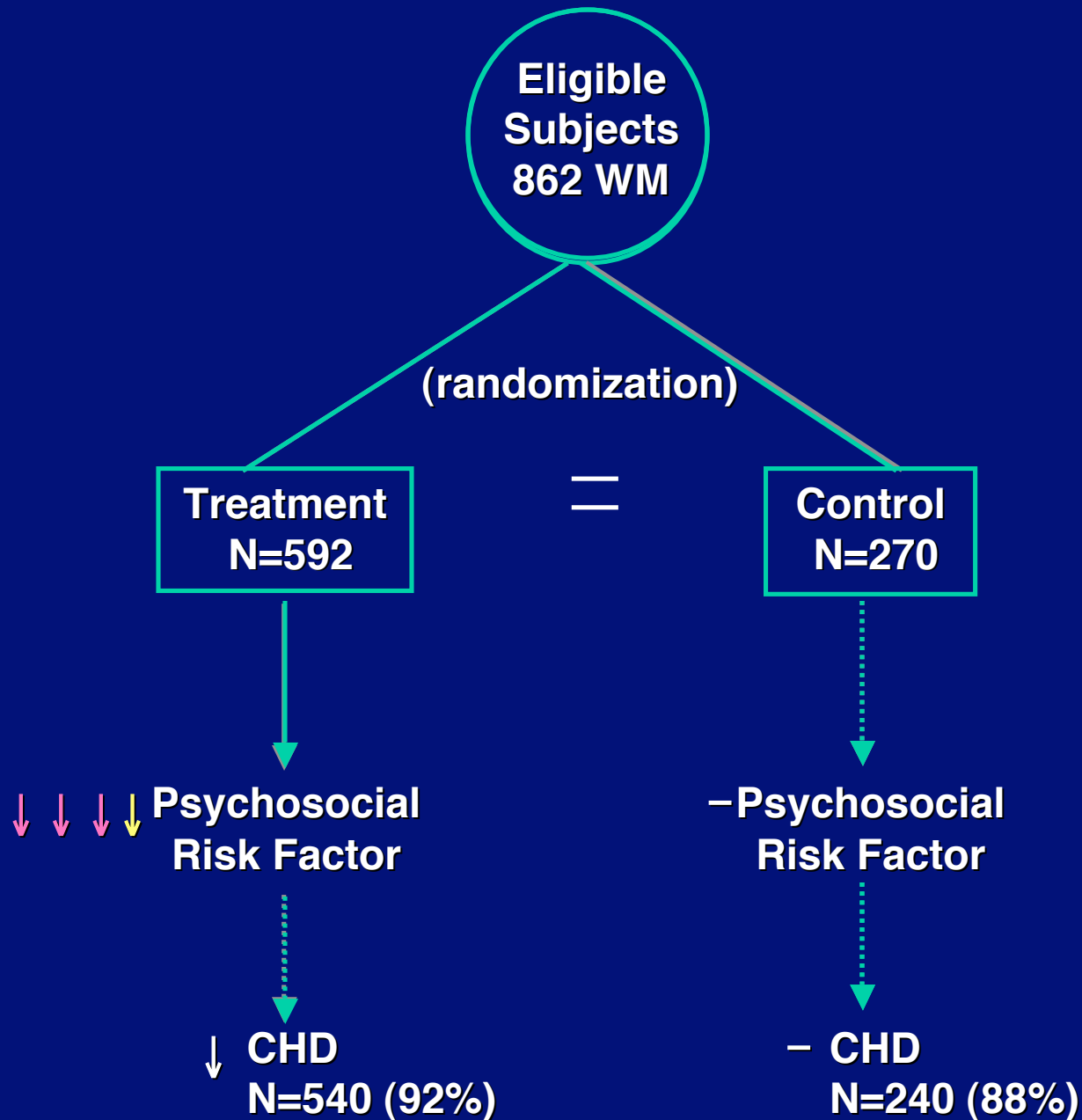
*** $p < 0.001$

** $p < 0.01$

* $p < 0.05$

Mendes de Leon, Psychosom Med, 1991

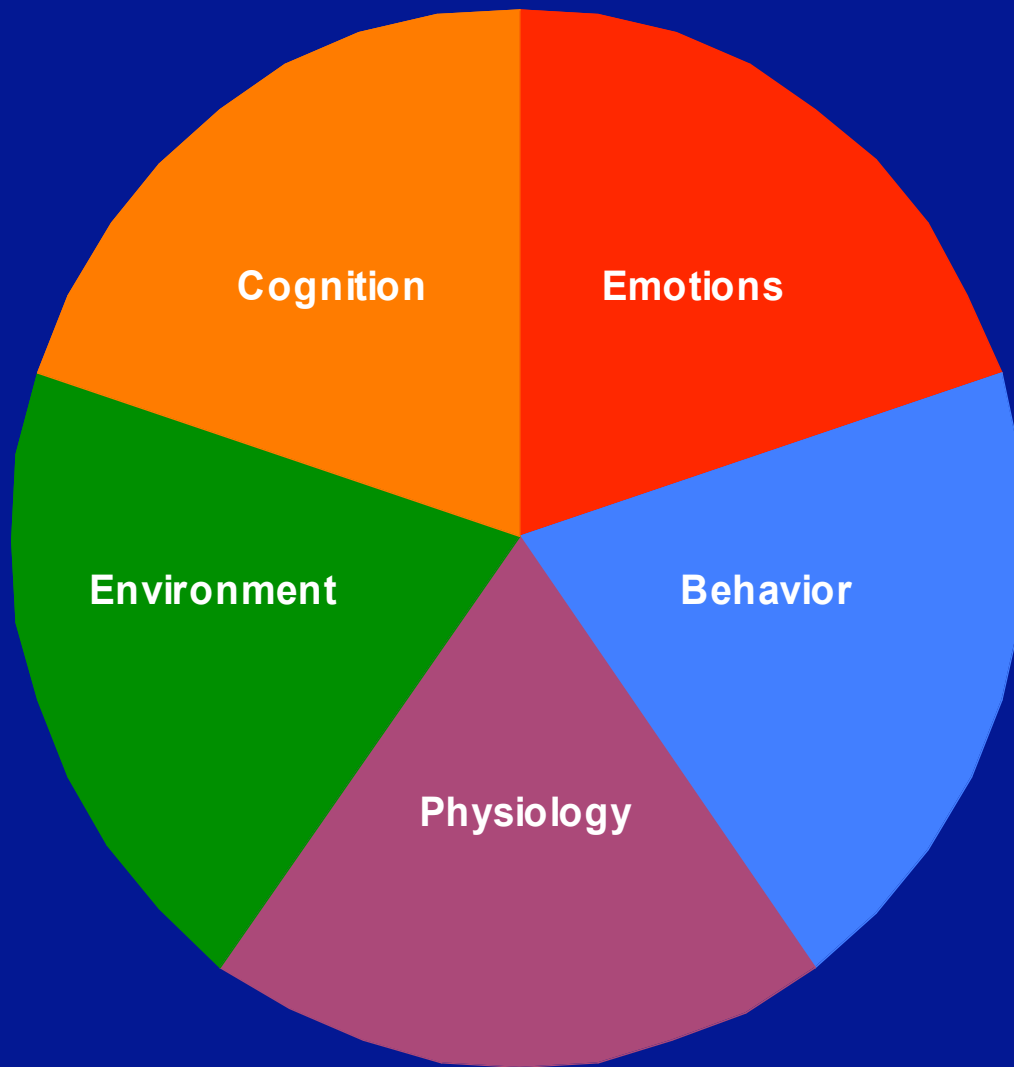
RCPP Clinical Trial Design



WHAT WE LEARNED

- Value of strong and long intervention.
- Many things change. Intended target may not be the real mechanism for effectiveness.
- Initiate sustained change by changing specific behavior.

Reciprocal Determinism

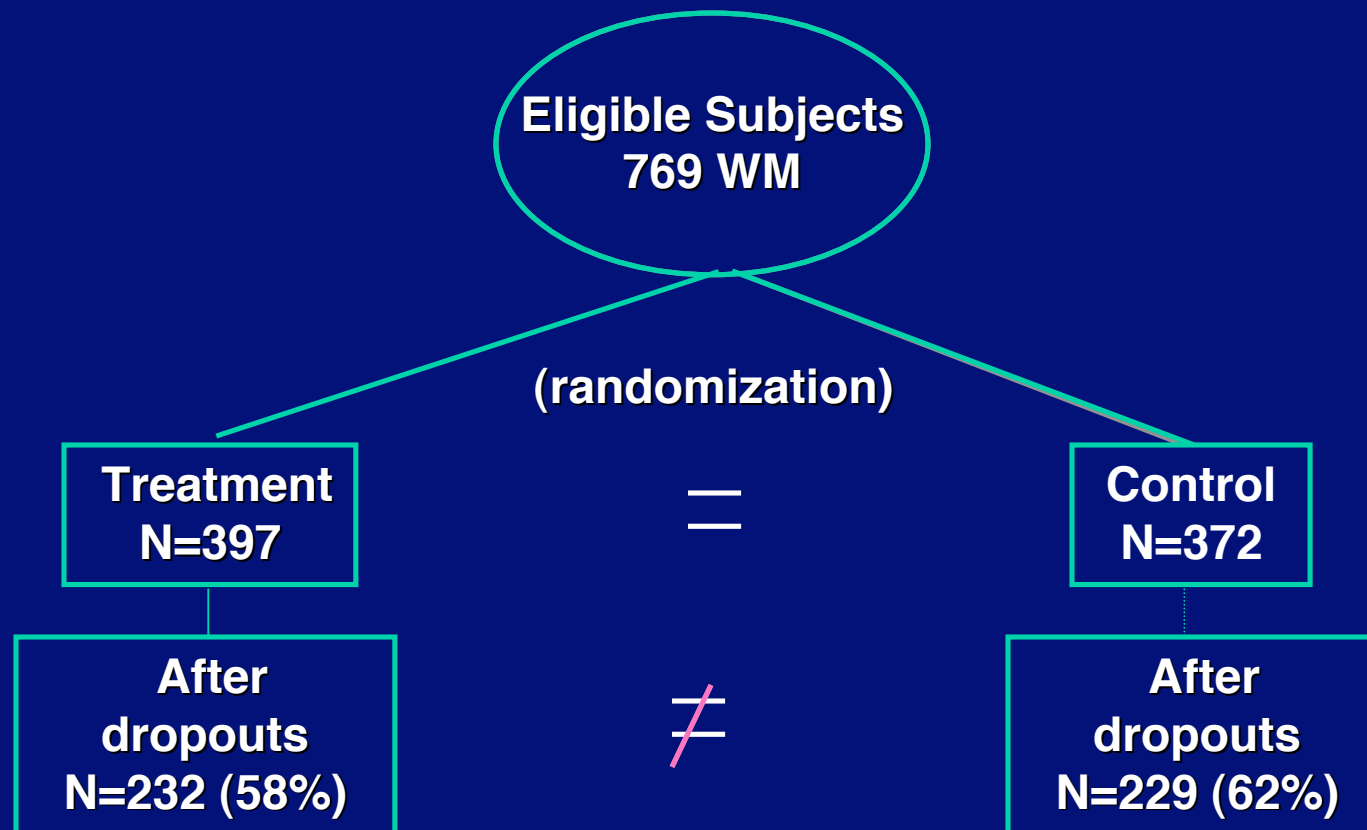


The Ischemic Heart Disease Stress Monitoring Trial 1983-1986

Principal Investigator: Nancy Frasure-Smith, PhD

HYPOTHESIS: The provision of emotional support at a time of high vulnerability to stress results in a reduction in cardiac deaths or nonfatal MI in *male* post-MI patients.

IHD Stress Monitoring Clinical Trial Design



IHD Stress Monitoring Trial: Baseline Comparability

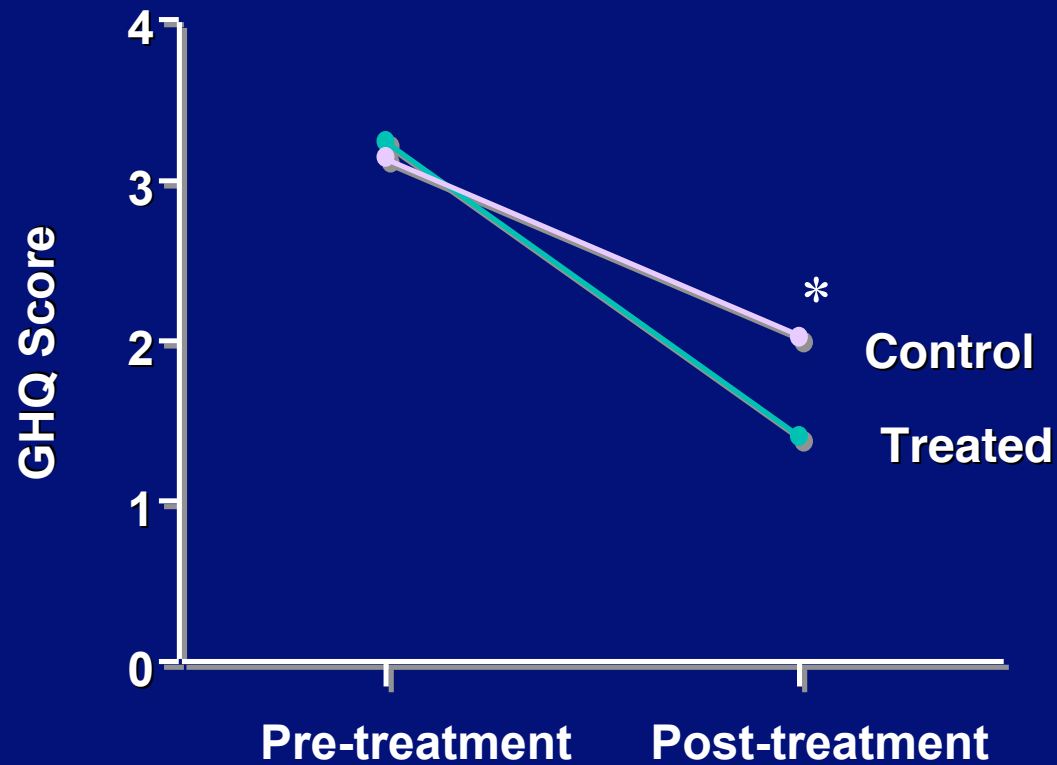
	Treatment	Control
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Education	↑	↓
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Occupation: White Collar	↑	↓
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Income	↑	↓
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Reduction in Distress at 1-Year Follow-up



* $p < 0.05$

Frasure-Smith & Prince,
1985

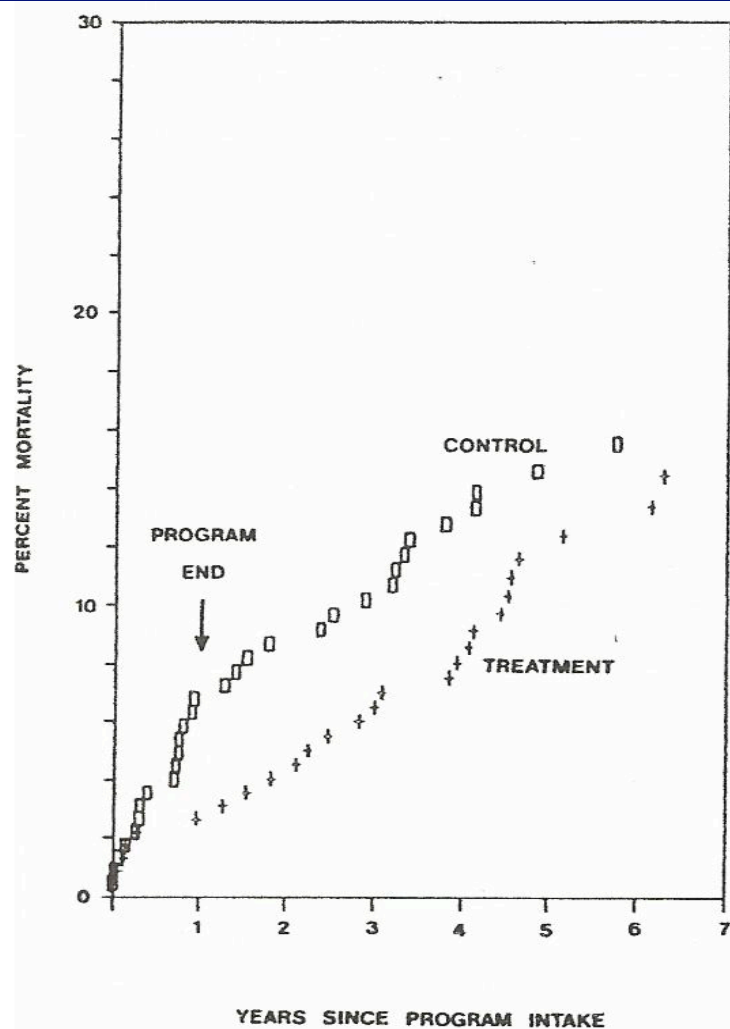


Fig. 2. Cumulative out-of-hospital mortality (sudden deaths) in the treatment and control groups.

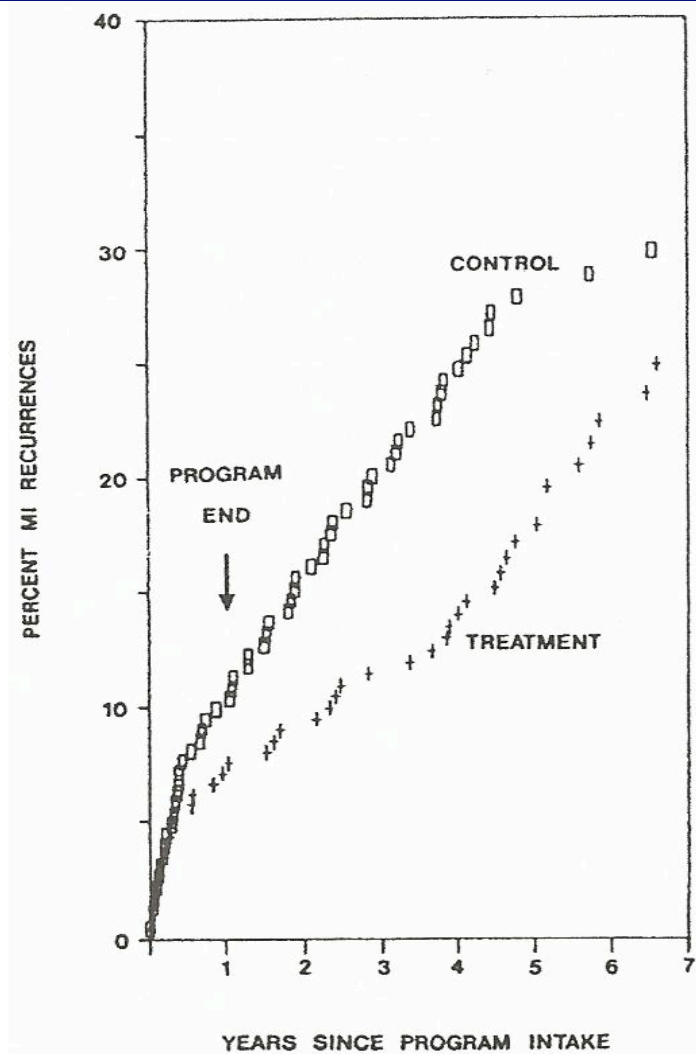
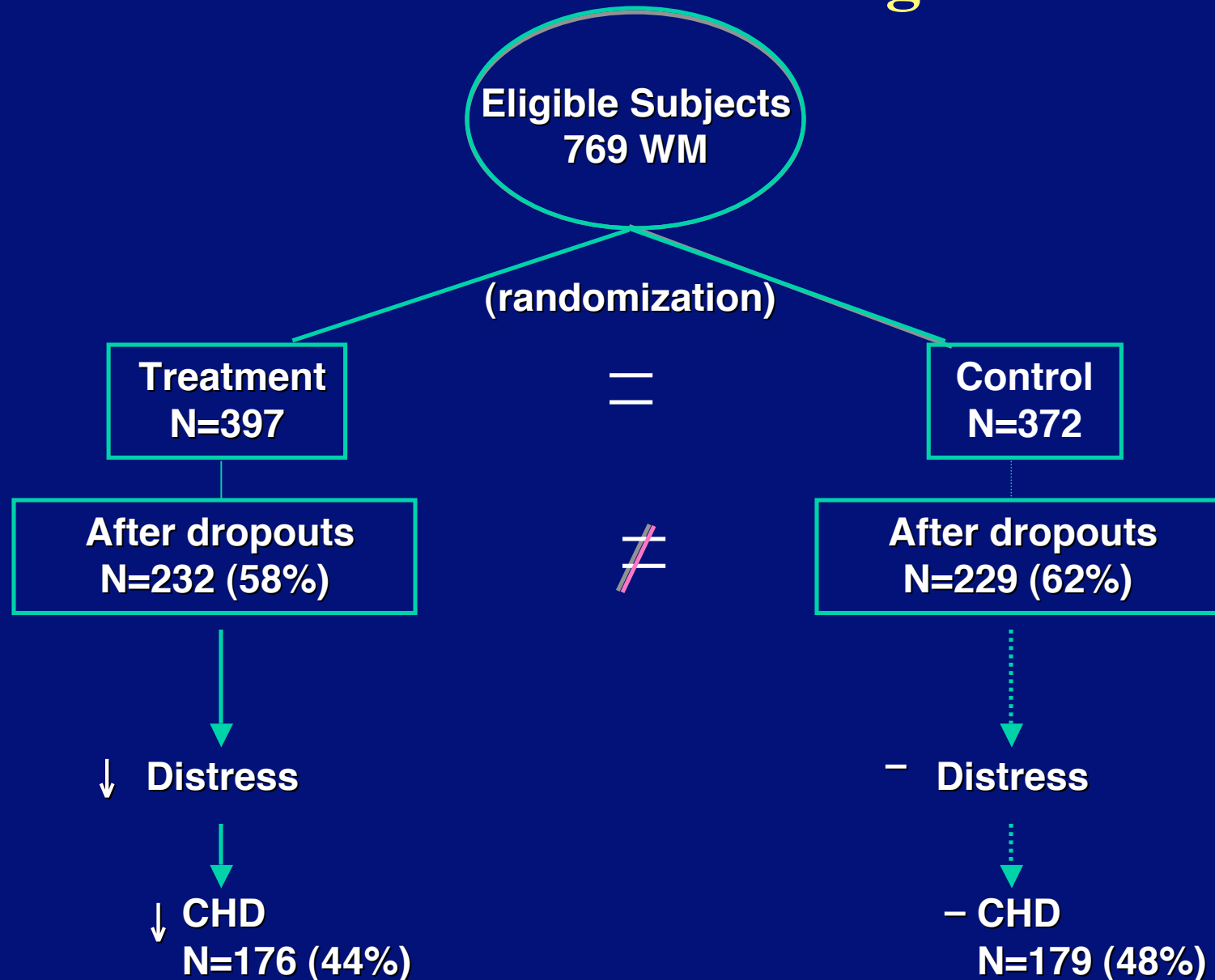


Fig. 3. Cumulative MI recurrences in the treatment and control groups.

IHD Stress Monitoring Clinical Trial Design



WHAT WE LEARNED

- Guard the randomization throughout the trial.
- Participants respond rationally to their preferences for treatment.

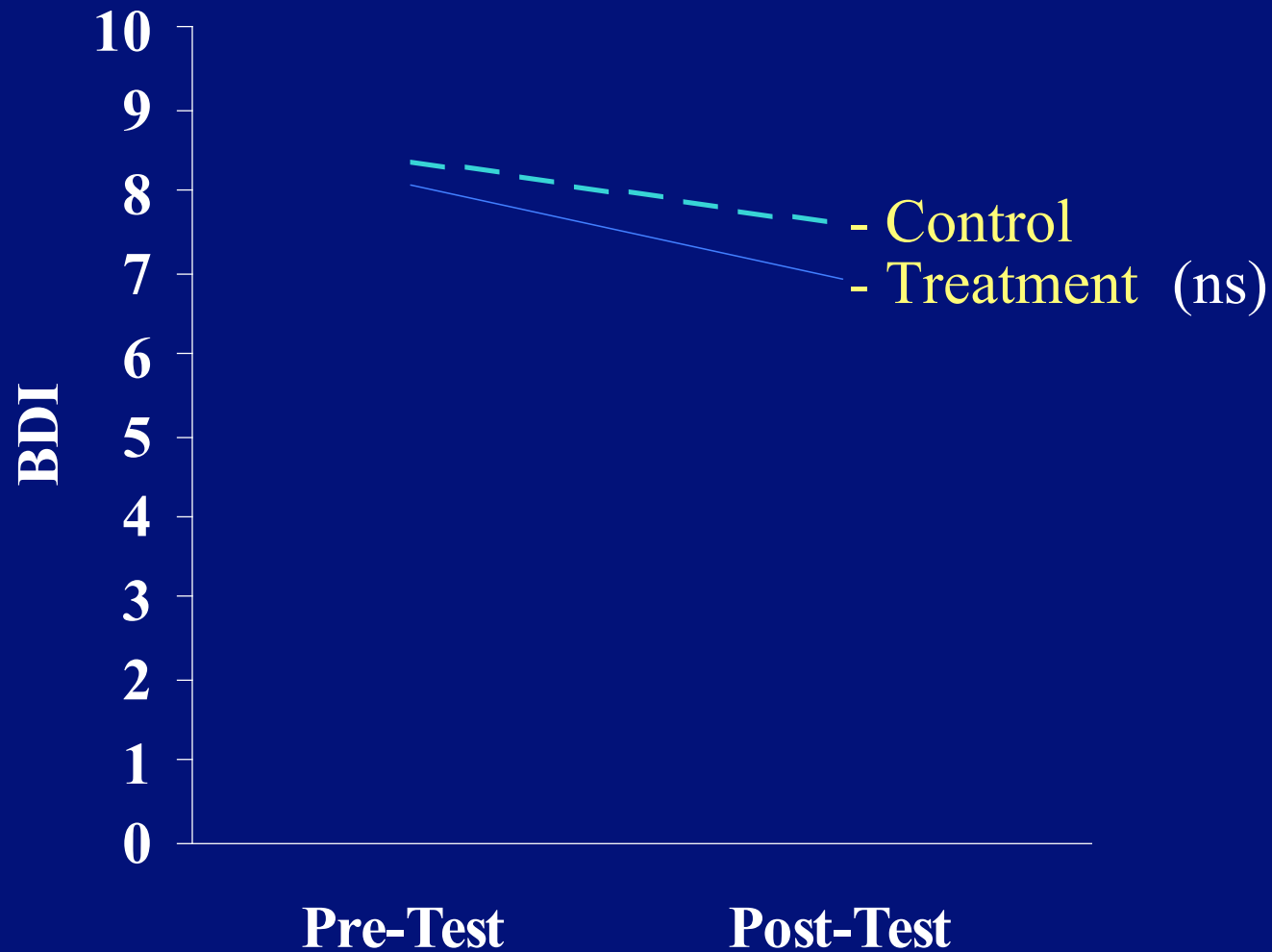
Montreal Heart Attack Readjustment Trial (M-HART) 1992-1997

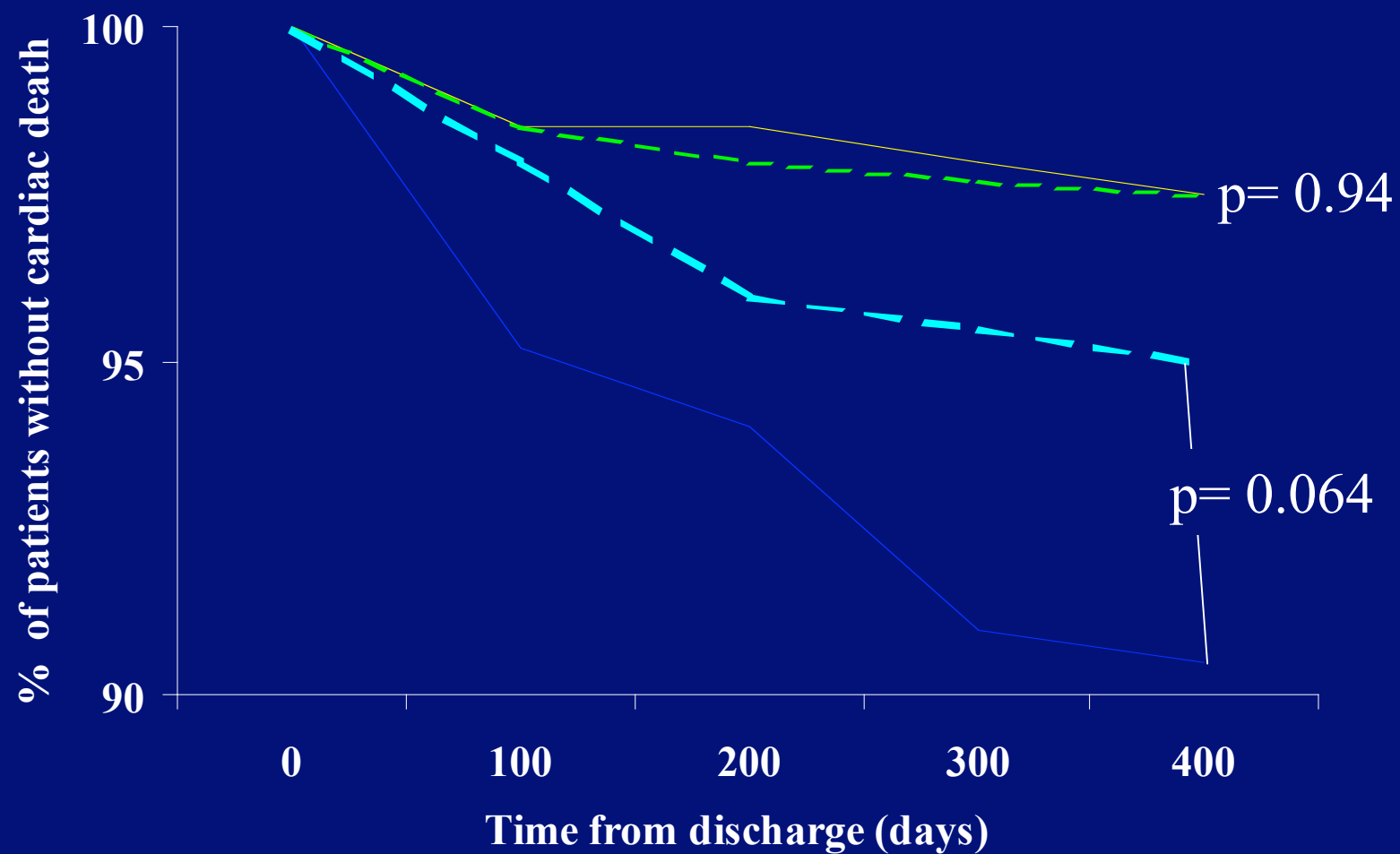
Principal Investigator: Nancy Frasure-Smith, PhD

HYPOTHESIS:

- The provision of emotional support at a time of high vulnerability to stress results in a reduction in cardiac deaths or nonfatal MIs in *male and female* post-MI patients.

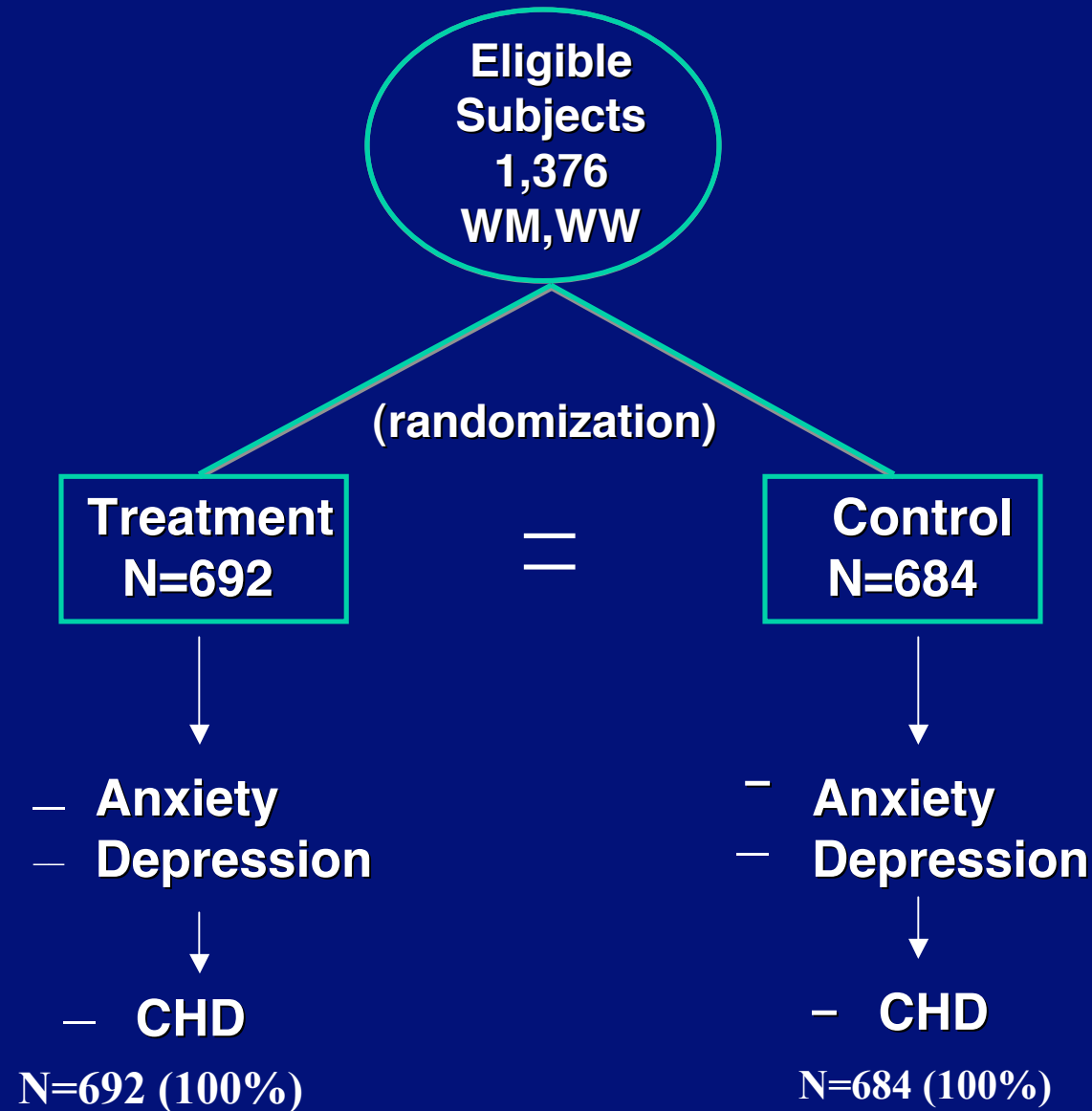
M-HART Change in Depression





— Intervention men (n=458)	- - Control men (n=445)
— Intervention women (n=234)	- - Control women (n=239)

M-HART Clinical Trial Design



WHAT WE LEARNED

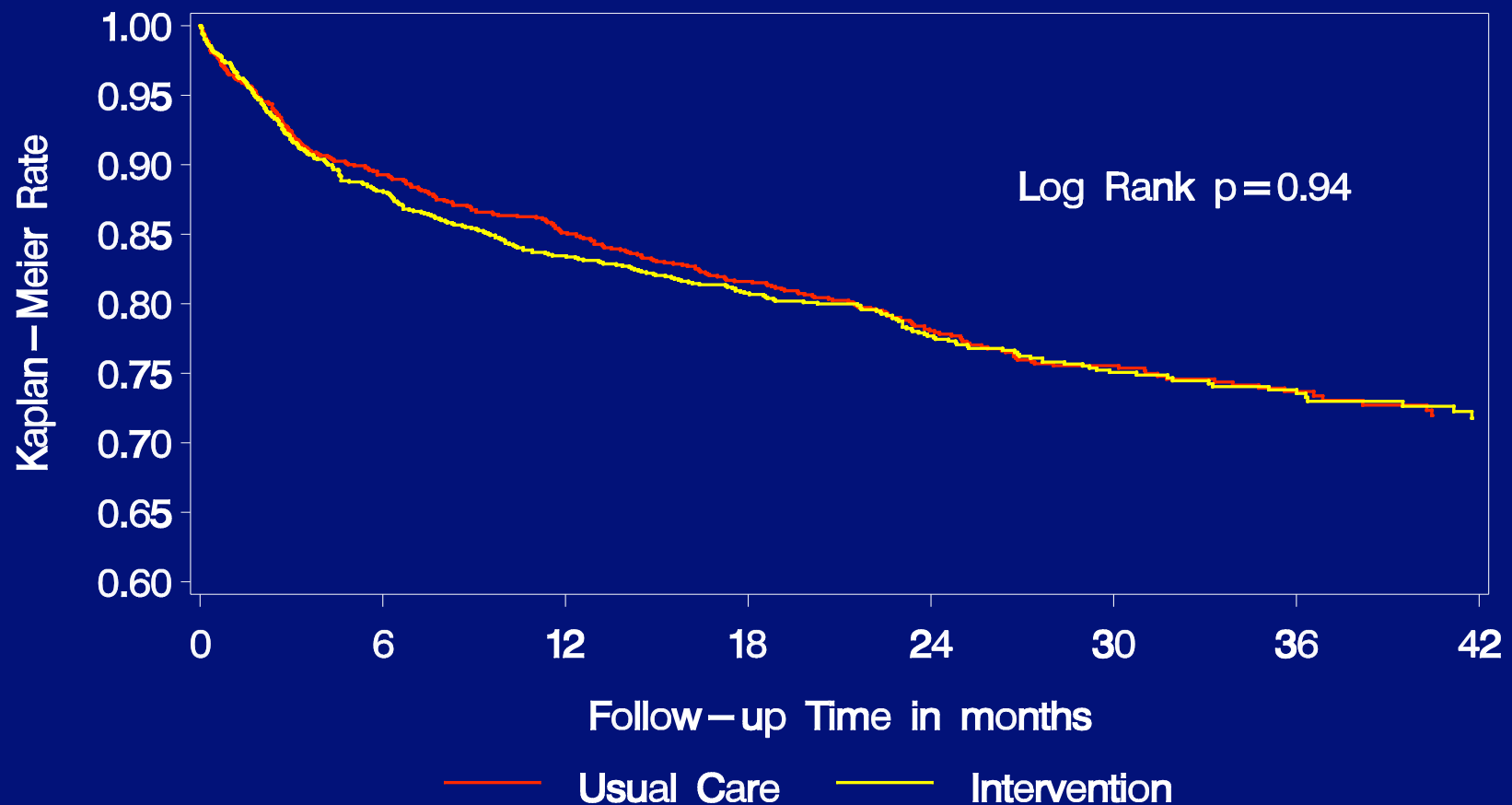
- Replication is essential in medicine.
- Behavioral treatments *can* harm.

Enhancing Recovery in Coronary Heart Disease (ENRICHD) Trial 1996-2003

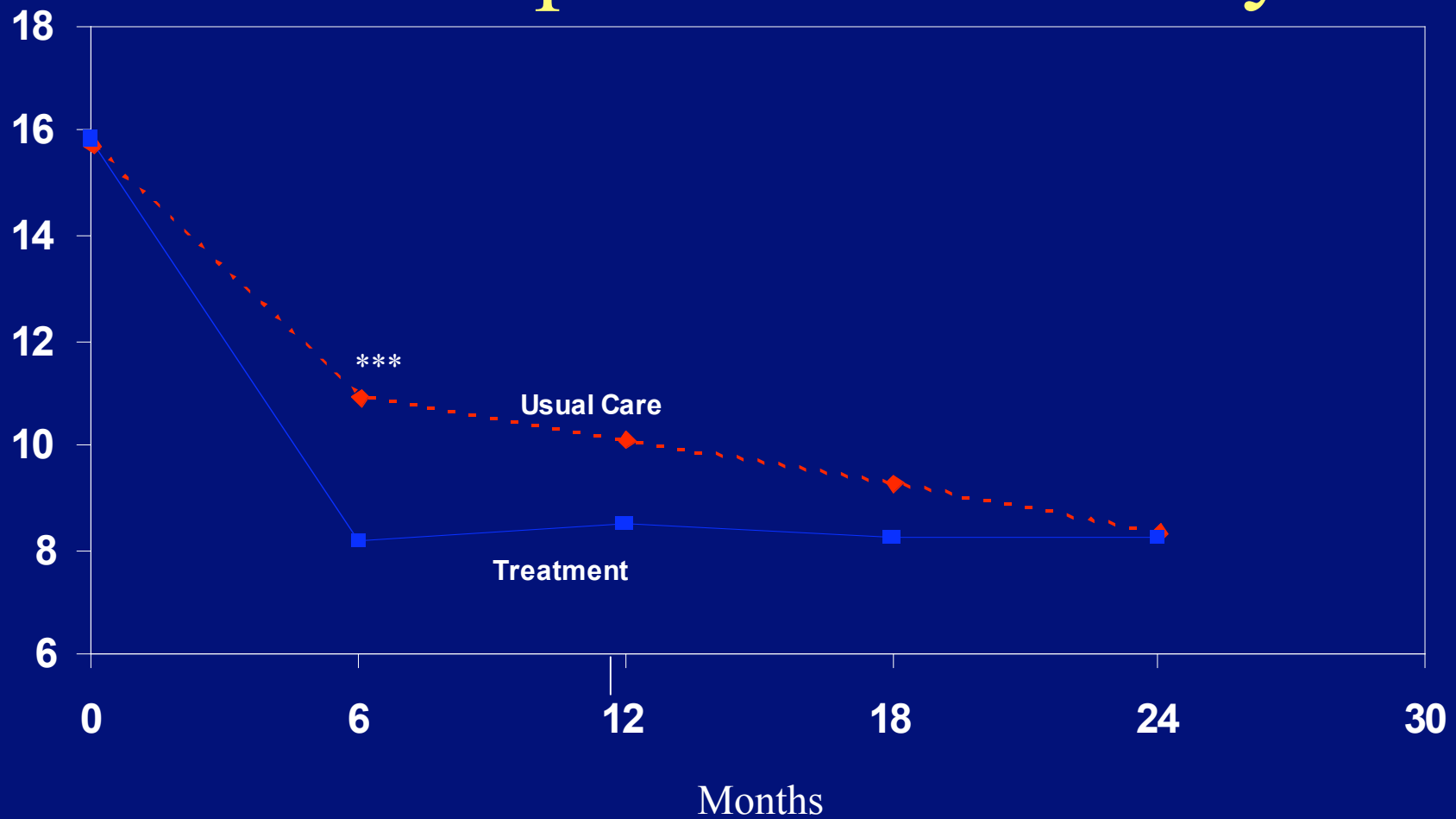
Principal Investigator: The ENRICHD Investigators

HYPOTHESIS: In post-MI patients who are depressed or have low social support, reduction in these psychosocial factors will reduce mortality or nonfatal MI.

Kaplan-Meier Survival Curves



Beck Depression Inventory

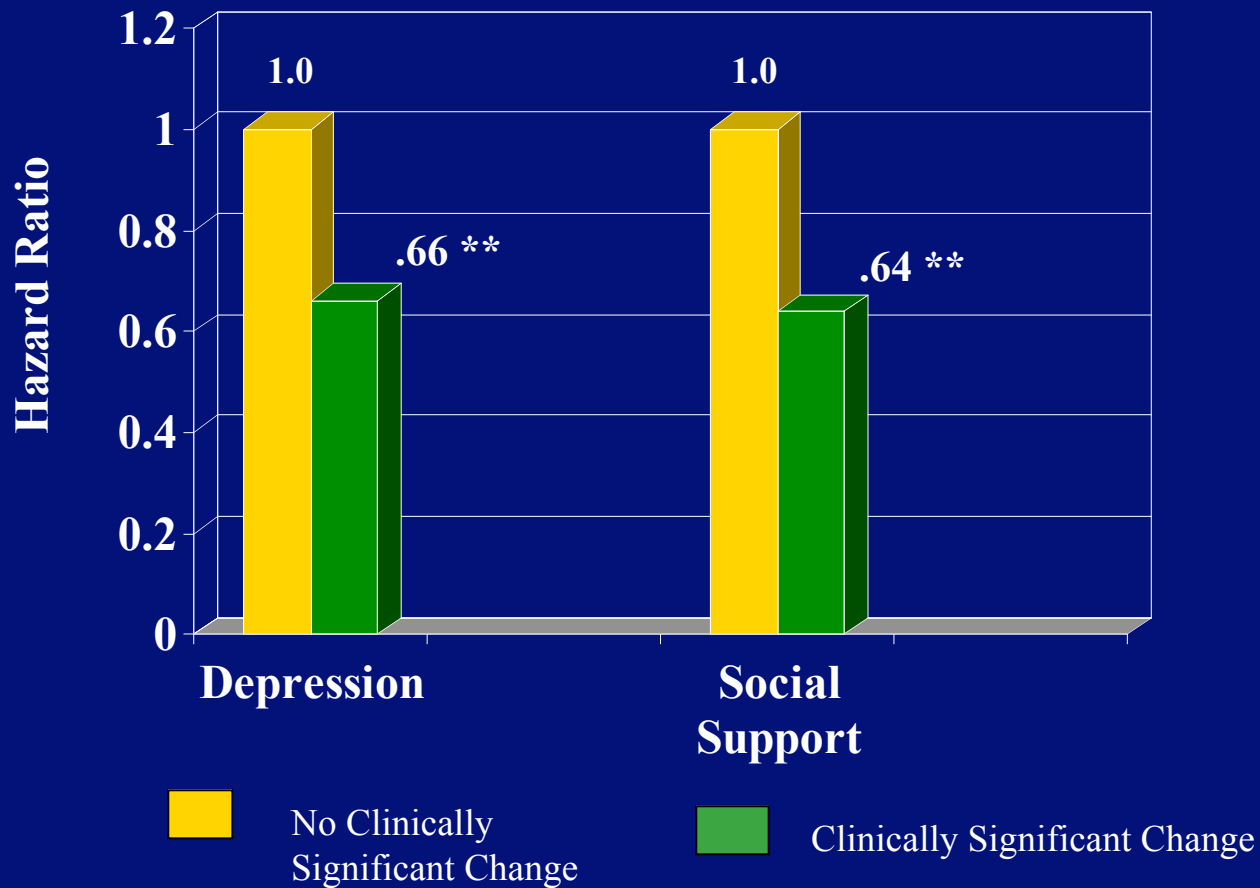


Treatment

Follow - up

*** $p < 0.001$

ENRICHD: Clinically Significant Behavior Change and Risk of Death or Non-Fatal MI

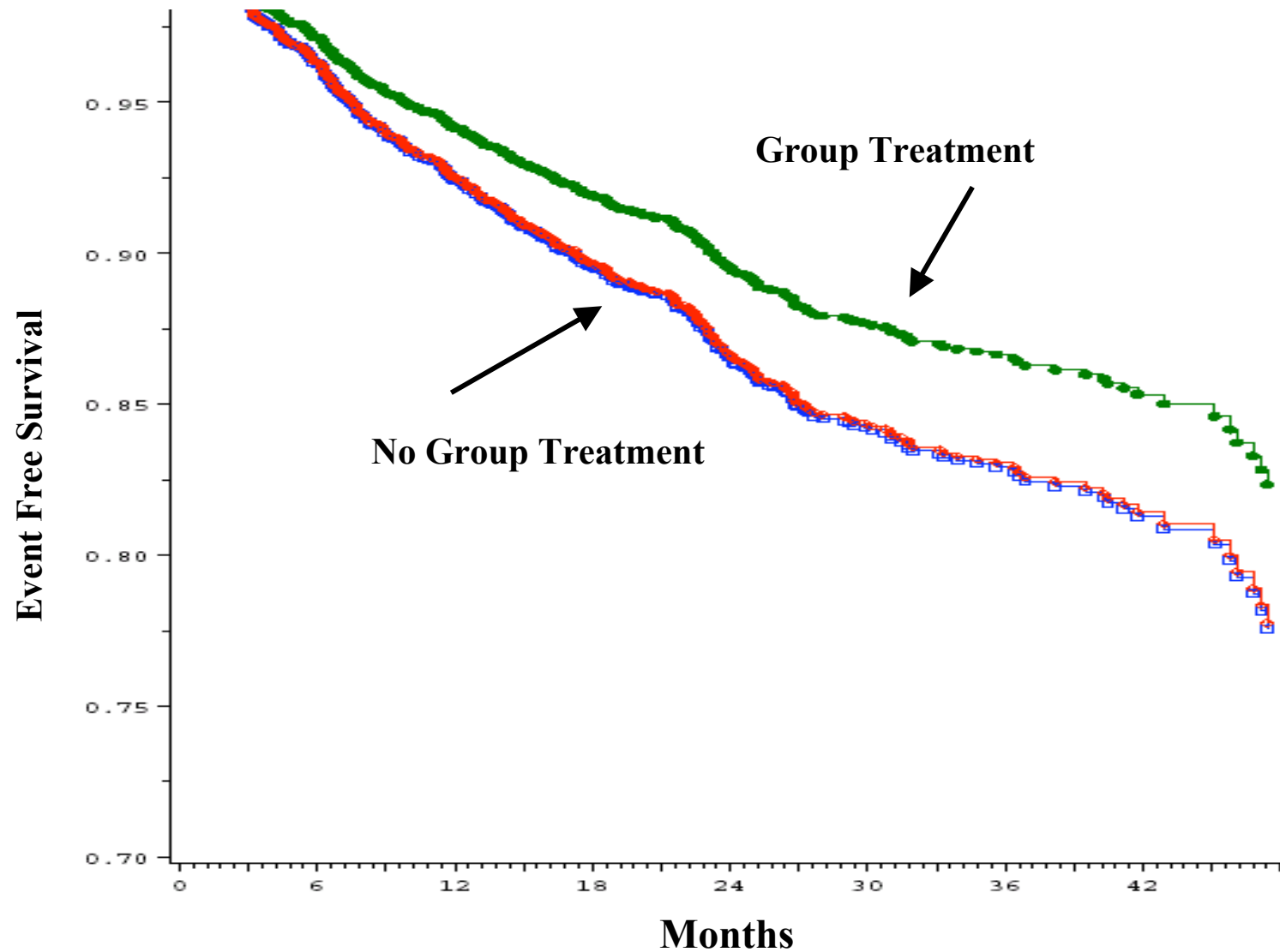


ENRICHHD: Primary Endpoint

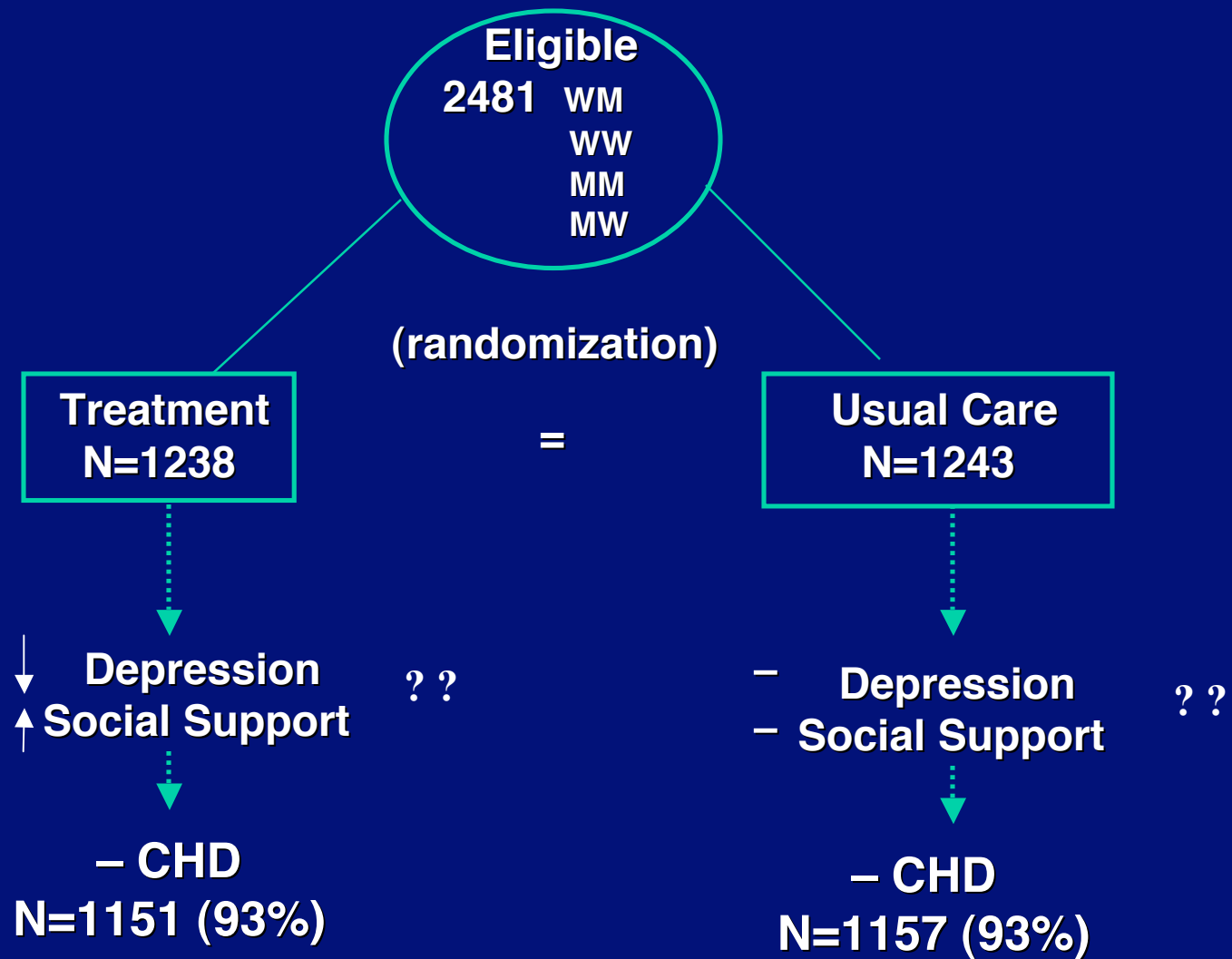


ENRICHD

COMPARISON OF THOSE WHO DID AND DID NOT RECEIVE GROUP TREATMENT



ENRICHD



WHAT WE LEARNED

- Value of strong intervention.
- One size may not fit all. Understand cultural variability in response to treatment.
- Coping peers are effective change agents.

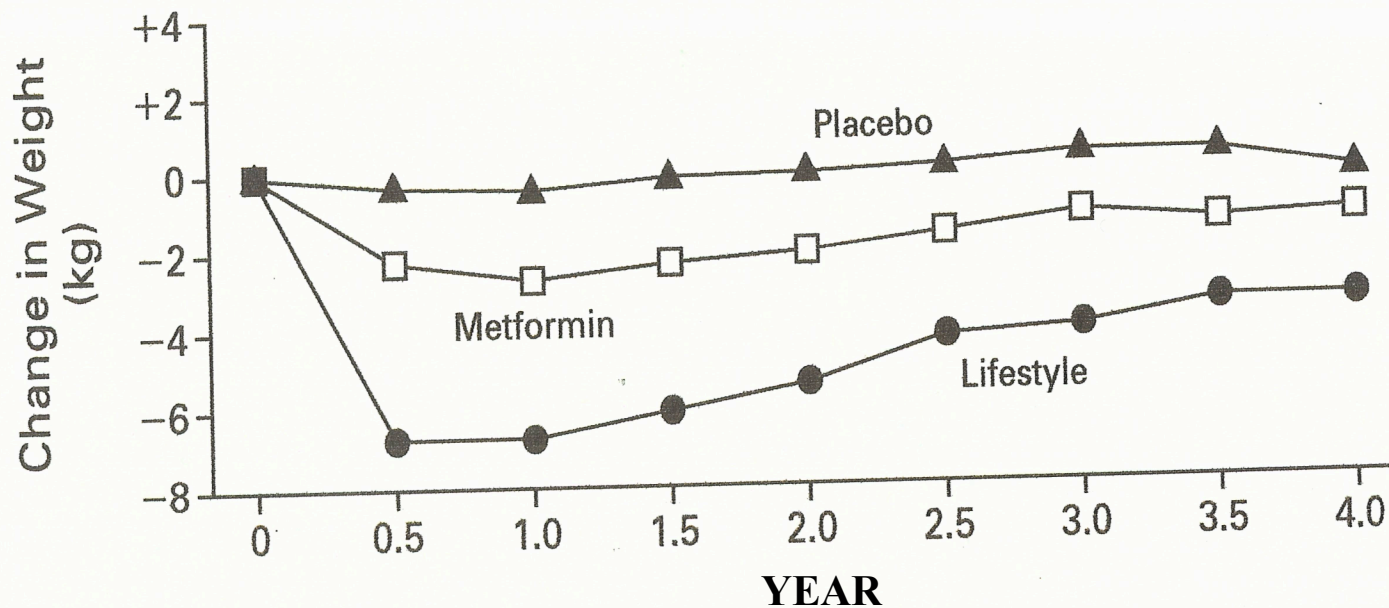
The Diabetes Prevention Program 1996-2001

Principal Investigator:

Diabetes Prevention Program Research Group

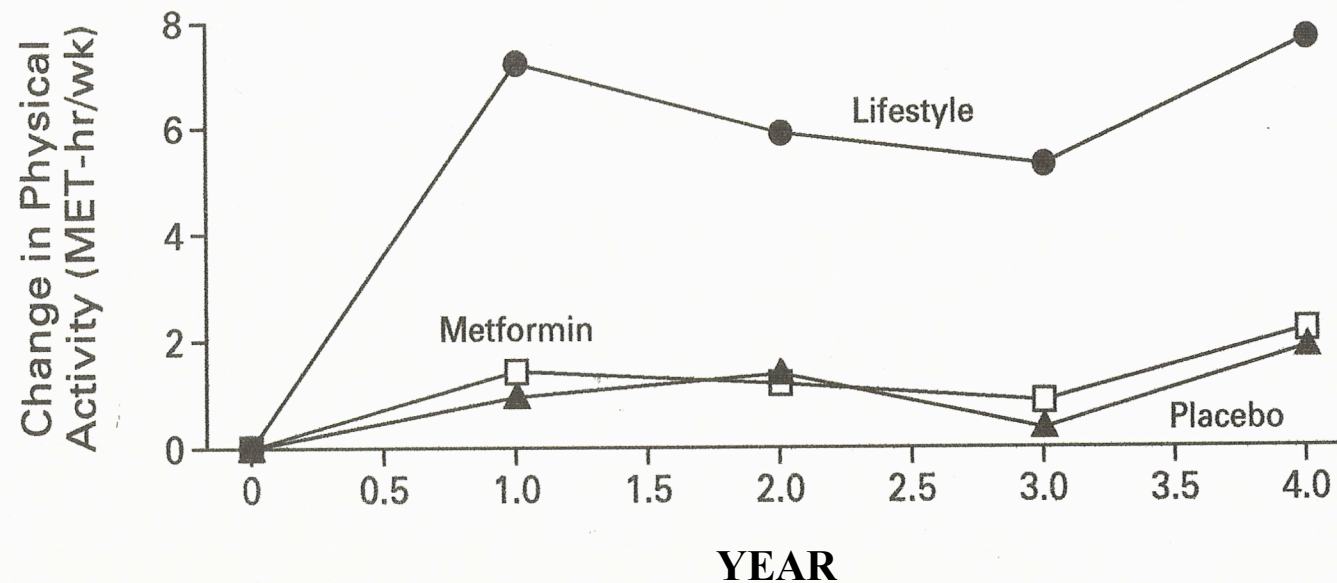
HYPOTHESIS: Modification of overweight and sedentary lifestyle prevents or delays the development of diabetes in high-risk patients.

DPP: Change in Weight



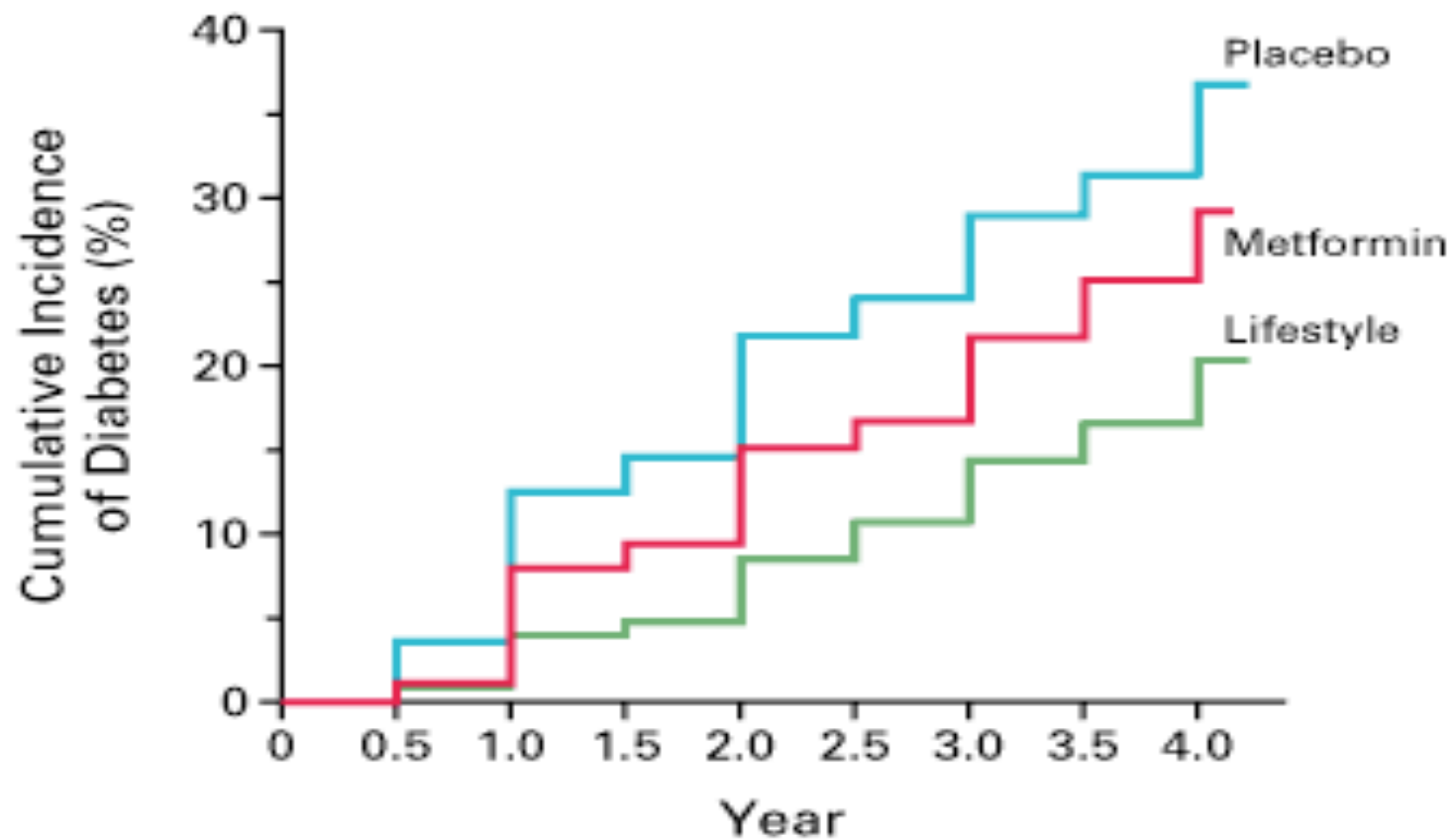
— Treatment Follow-up

DPP: Change in Physical Activity

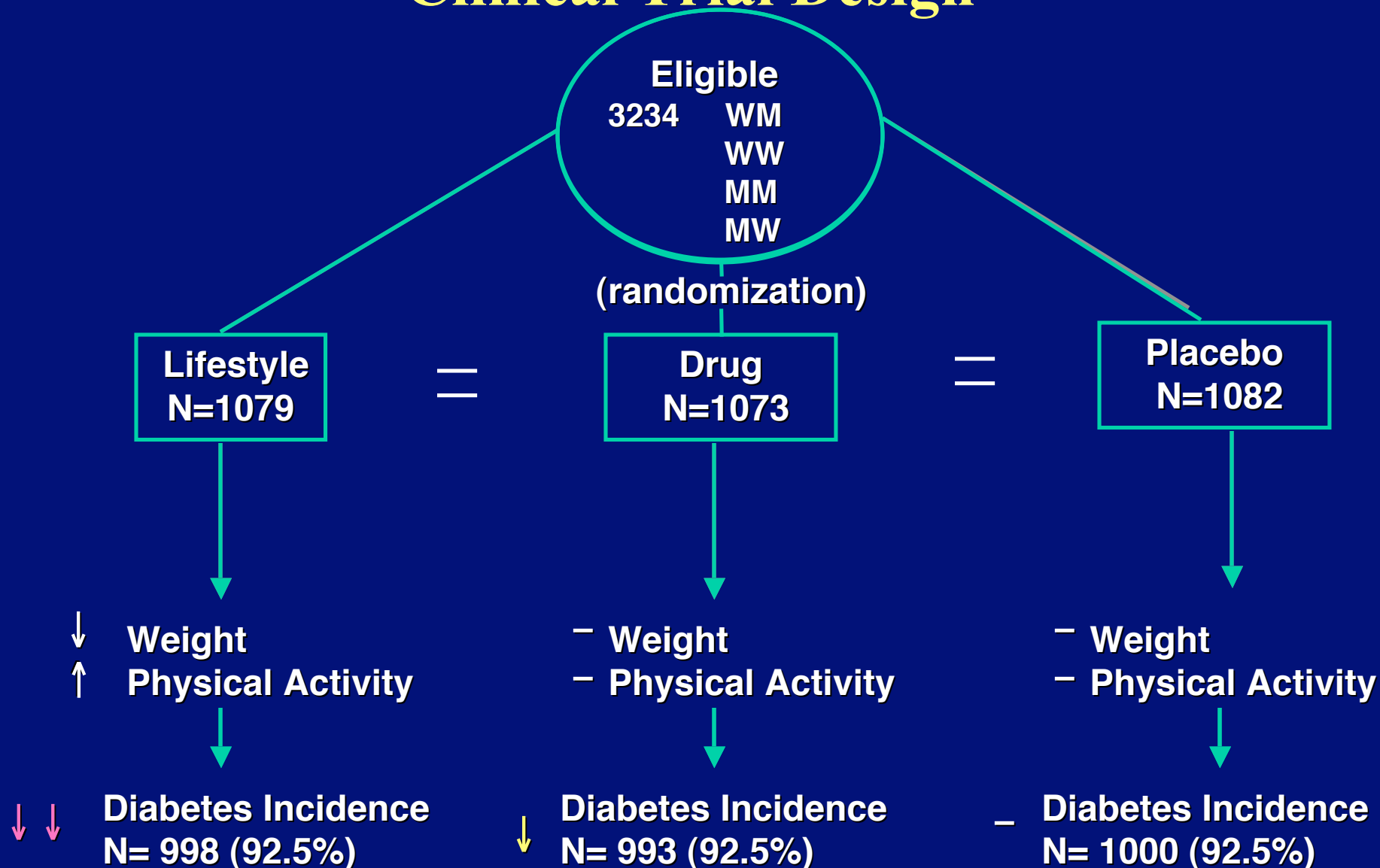


— Treatment Follow-up

DPP: Incidence of Diabetes



Diabetes Prevention Program Clinical Trial Design



What We Learned

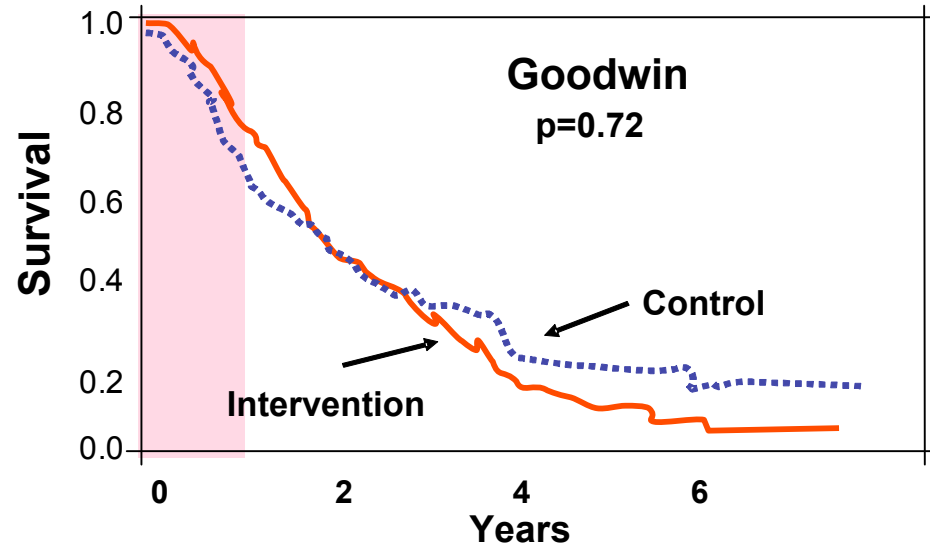
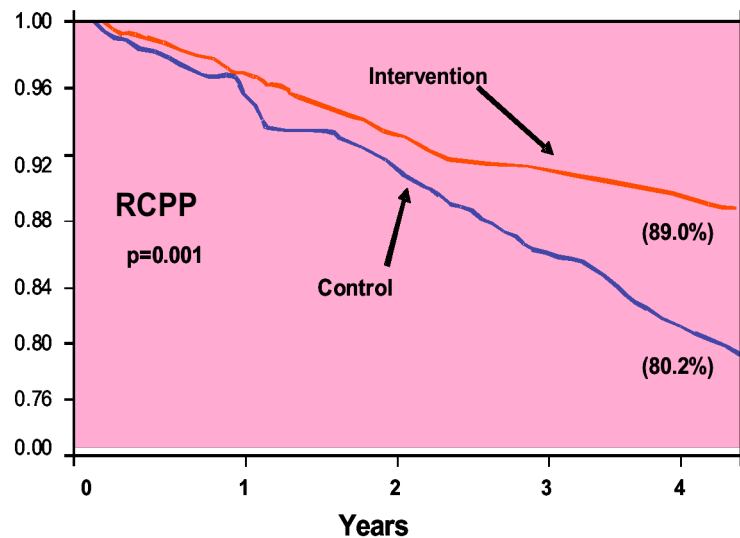
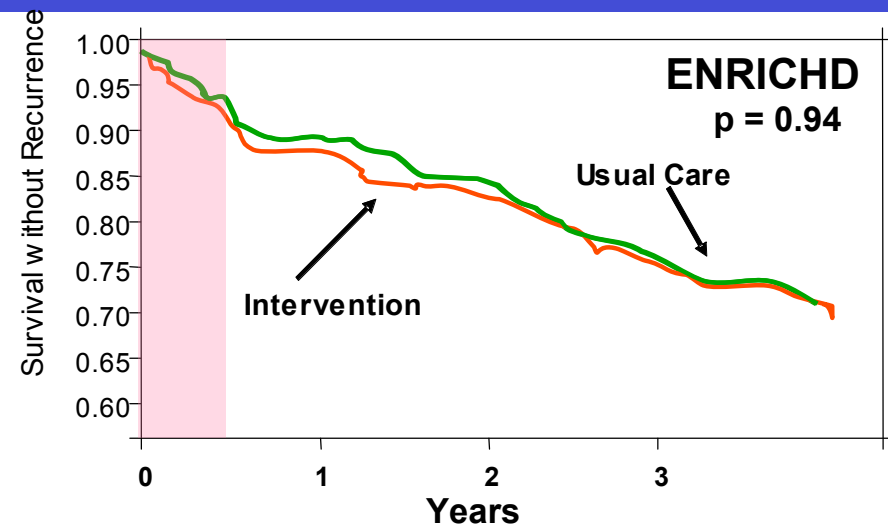
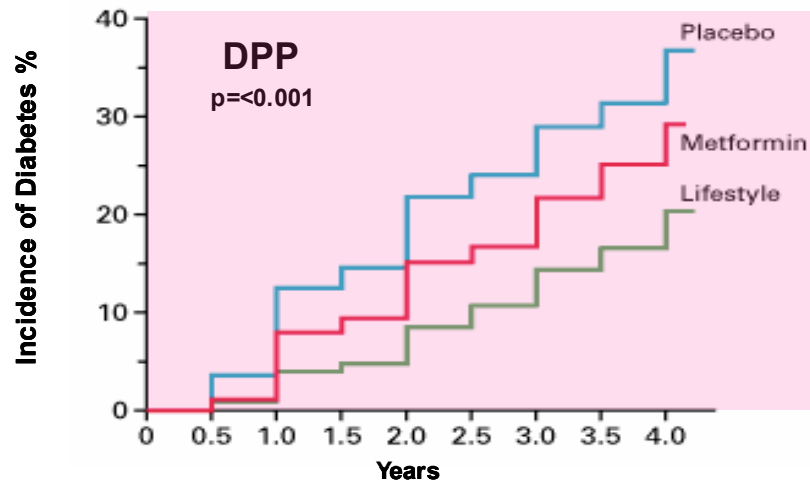
- Value of a simple message and simple goals.
- Importance of maintenance activities.

Trial Success by Duration of Treatment

(duration in pink)

Successes

Failures



ADVERTISING

“Focus relentlessly on a simple, single message. Go into into the customer’s brain and attach one brightly-colored phrase to it.”

(Schultz, *Essentials of Advertising*, 1996)

POLITICS

“Stay on message. Resist temptation to overload the system with too many messages. Symbols speak louder than words.”

(Holbrook, *Do Campaigns Matter?* 1996)

MILITARY

“Pick your battles wisely. Throw your mass of forces on deciding points. Appeal to the strongest emotions.”

(Bevin, *How Great Generals Win*, 1993)



SAVE
ENERGY

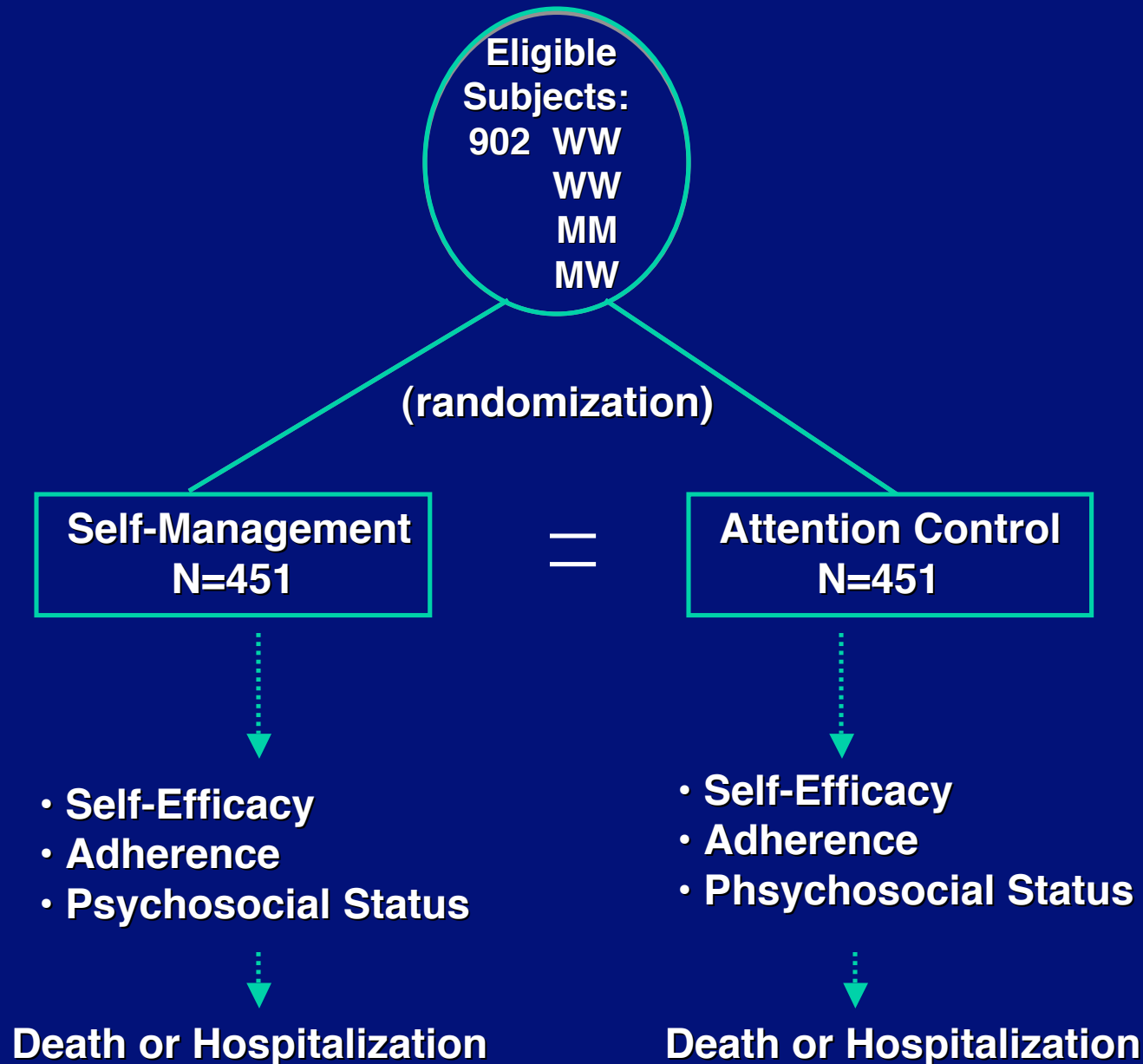
WASTE
ENERGY

The Heart Failure Adherence and Retention Trial (HART)

**Principal Investigator: Lynda H. Powell, PhD
2001 - Present**

Purpose: To determine whether group-based self-management training will reduce death or hospitalization in patients with Class II or III heart failure.

HART Clinical Trial Design



The Data and Safety Monitoring Committee:

Competitor or Collaborator?

Comments from the DSMB:

“HART seems to be making good progress. You have identified the problem areas and seem to have reasonable solutions. It takes a long time to change the course of a large ship, but I sense that this is beginning to happen.”

Patient Discovery

(HART Focus Group Participant:)

“...I think I eat much better than before I started coming to the group... and I can feel the difference. I couldn't even walk from the front door to here... It's surprising how, **when you change what you eat, how much better you feel.**”

ISSUE: Choice of Appropriate Control Group

Usual Care:

To determine treatment efficacy over the standard of care.

Attention Control:

To determine whether treatment was efficacious over the simple provision of attention.

ISSUE: Poorer attendance early in treatment in the disadvantaged minorities results in differential exposure to full treatment package.

Make-up sessions for missed meetings in later phase of treatment may minimize differential exposure to treatment by ethnicity.

SUMMARY

The randomized clinical trial focusing on **important clinical outcomes** is the language of medicine. Behavioral scientists must become fluent in this language.

SUMMARY

Guard the randomization: Once randomized, always analyzed. This is the only control for unmeasured confounders.

SUMMARY

The single most important challenge for behavioral science is how to produce **sustained change in lifestyle**. Interventions should be strengthened by:

- Increasing their length;
- Simplifying their goals;
- Improving their cultural sensitivity;
- Promoting discovery.

SUMMARY

A behavioral intervention can harm.

Pilot the intervention and understand
diversity in response before
undertaking an efficacy trial.